

IN THE CLAIMS:

1. (Currently Amended) A method of detecting a difference of one or more nucleotides between a nucleic acid molecule to be tested and a reference nucleic acid molecule, said method comprising subjecting the test nucleic acid molecule to single-base-specific cleavage to generate oligonucleotide fragments, separating the resulting oligonucleotide fragments based on mass by MALDI-TOF MS or other equivalent procedure to produce a fingerprint of the oligonucleotide fragments comprising one or more peaks wherein a peak represents the mass of each fragment and identifying an altered peak relative to a reference nucleic acid molecule subjected to the same procedure wherein the presence of an altered peak is indicative of a difference of one or more nucleotides in said tested nucleic acid molecule.
2. (Original) A method according to claim 1 wherein the nucleic acid molecule to be tested is amplified by a polymerase chain reaction (PCR) prior to base specific cleavage.
3. (Previously Presented) A method according to claim 1 wherein the base specific cleavage results in oligonucleotide fragments of from about 2 bases to about 1000 bases.
4. (Original) A method according to claim 3 wherein the base specific cleavage results in oligonucleotide fragments of from about 3 bases to about 500 bases.
5. (Original) A method according to claim 4 wherein the base specific cleavage results in oligonucleotide fragments of from about 4 bases to about 100 bases.
6. (Previously Presented) A method according to claim 1 wherein the base specific cleavage is uracil specific cleavage.
7. (Original) A method according to claim 6 wherein the uracil specific cleavage is mediated by uracil-N-glycosylase.

8. (Previously Presented) A method according to claim 1 further comprising subjecting fragmentation products to further separation (PSD) to generate a spectrum from decay dependent on the nucleotide sequence of the oligonucleotide.
9. (Original) A method according to claim 8 wherein the further separation of fragmentation products is by post source decay (PSD).
10. (Currently Amended) A computer program which controls a method of detecting a difference of one or more nucleotides between a nucleic acid molecule to be tested and a reference nucleic acid molecule, said method comprising subjecting the test nucleic acid molecule to single-base-specific cleavage to generate oligonucleotide fragments, separating the resulting oligonucleotide fragments based on mass by MALDI-TOF MS or other equivalent procedure to produce a fingerprint of the oligonucleotide fragments comprising one or more peaks wherein a peak represents the mass of each fragment and identifying an altered peak relative to a reference nucleic acid molecule subjected to the same procedure, wherein the presence of an altered peak is indicative of a difference of one or more nucleotides in said tested nucleic acid molecule.
11. (Original) A method according to claim 9 wherein the nucleic acid to be tested is amplified by PCR prior to base specific cleavage.
12. (Previously Presented) A method according to claim 9 wherein the base specific cleavage results in oligonucleotide fragments of from about 2 bases to about 1000 bases.
13. (Original) A method according to claim 9 wherein the base specific cleavage results in oligonucleotide fragments of from about 3 bases to about 500 bases.
14. (Original) A method according to claim 10 wherein the base specific cleavage results in oligonucleotide fragments of from about 4 bases to about 100.

15. (Previously Presented) A method according to claim 9 wherein the base specific cleavage is uracil specific cleavage.

16. (Original) A method according to claim 14 wherein the uracil specific cleavage is mediated by uracil-N-glycosylase.

17. (Previously Presented) A method according to claim 10 further comprising the further separation of fragmentation products to generate a spectrum form decay dependent on the nucleotide sequence of the oligonucleotide.

18. (Original) A method according to claim 17 wherein the further separation of fragmentation products is by post source decay (PSD).

19-23. (Previously cancelled)

19 24. (Currently Amended) A method for identifying or locating a mutation in one or more bases in a target nucleic acid molecule, comprising subjecting the target nucleic acid molecule to single-base-specific cleavage to generate oligonucleotide fragments, separating the resulting oligonucleotide fragments based on mass by MALDI-TOF MS ~~or other equivalent procedure~~ to produce a fingerprint of the oligonucleotide fragments comprising one or more peaks wherein a peak represents the mass of each fragment, and identifying an altered peak relative to a reference nucleic acid molecule subjected to the same procedure, wherein the presence of an altered peak is indicative of a mutation in one or more bases in said target nucleic acid molecule.

20 25. (Original) A method according to claim 24 ¹⁹ wherein the nucleic acid molecule to be tested is amplified by a polymerase chain reaction (PCR) prior to base specific cleavage.

21 26. (Previously Presented) A method according to claim 24 ¹⁹ wherein the base specific cleavage results in oligonucleotide fragments of from about 2 bases to about 1000 bases.

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27. (Original) A method according to claim 26 wherein the base specific cleavage results in oligonucleotide fragments of from about 3 bases to about 500 bases.

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28. (Original) A method according to claim 27 wherein the base specific cleavage results in oligonucleotide fragments from about 4 bases to about 100 bases.

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29. (Previously Presented) A method according to claim 24 wherein the base specific cleavage is uracil specific cleavage.

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30. (Original) A method according to claim 29 wherein the uracil specific cleavage is mediated by uracil-N-glycosylase.

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31. (Previously Presented) A method according to claim 24 further comprising subjecting fragmentation products to further separation (PSD) to generate a spectrum from decay dependent on the nucleotide sequence of the oligonucleotide.

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32. (Original) A method according to claim 31 wherein the further separation of fragmentation products is by post source decay (PSD).

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33. (Currently Amended) A method of detecting a difference of one or more nucleotides between a nucleic acid molecule to be tested and a reference nucleic acid molecule, said method comprising subjecting the test molecule to single-base-specific cleavage to generate oligonucleotide fragments, separating the resulting oligonucleotide fragments based on mass by MALDI-TOF MS or other equivalent procedure to produce a fingerprint of the oligonucleotide fragments comprising one or more peaks wherein a peak represents the mass of each fragment, and identifying an altered peak relative to a reference nucleic acid molecule subjected to the same procedure, wherein the presence of an altered peak is indicative of said difference of one or more nucleotides, and wherein the difference does not result in a change of a cleavage site.

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34. (Previously Presented) A computer program which controls a method of detecting a difference of one or more nucleotides between a nucleic acid molecule to be tested and a

reference nucleic acid molecule, said method comprising subjecting the test nucleic acid molecule to single-base-specific cleavage to generate oligonucleotide fragments, separating the resulting oligonucleotide fragments to produce a fingerprint of the oligonucleotide fragments comprising one or more peaks wherein a peak represents the mass of each fragment and identifying an altered peak relative to a reference nucleic acid molecule subjected to the same procedure, wherein the presence of an altered peak is indicative of a difference of one or more nucleotides in said tested nucleic acid molecule, and wherein the difference does not result in a change of a cleavage site.

~~30~~ 35. (Currently Amended) A method for identifying or locating a mutation in one or more bases in a target nucleic acid molecule wherein the mutation does not result in a change of a cleavage site by a restriction enzyme, comprising subjecting the target nucleic acid molecule to single-base-specific cleavage to generate oligonucleotide fragments, separating the resulting oligonucleotide fragments based on mass by MALDI-TOF MS or other equivalent procedure to produce a fingerprint of the oligonucleotide fragments comprising one or more peaks wherein a peak represents the mass of each fragment, and identifying an altered peak relative to a reference nucleic acid molecule subjected to the same procedure, wherein the presence of an altered peak is indicative of a mutation in one or more bases in said target nucleic acid molecule, and wherein the difference does not result in a change of a cleavage site.